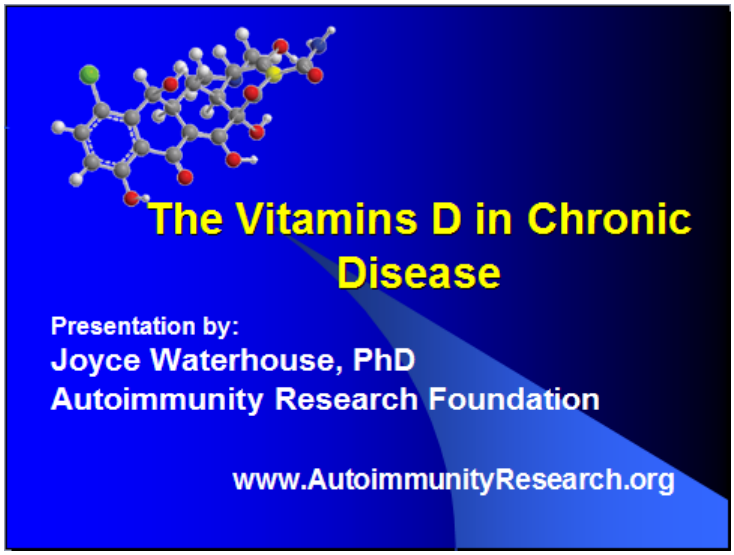


TRANSCRIPT OF 18 JUN 2006 PRESENTATION

Dr. Joyce Waterhouse

Vitamins D in Chronic Disease

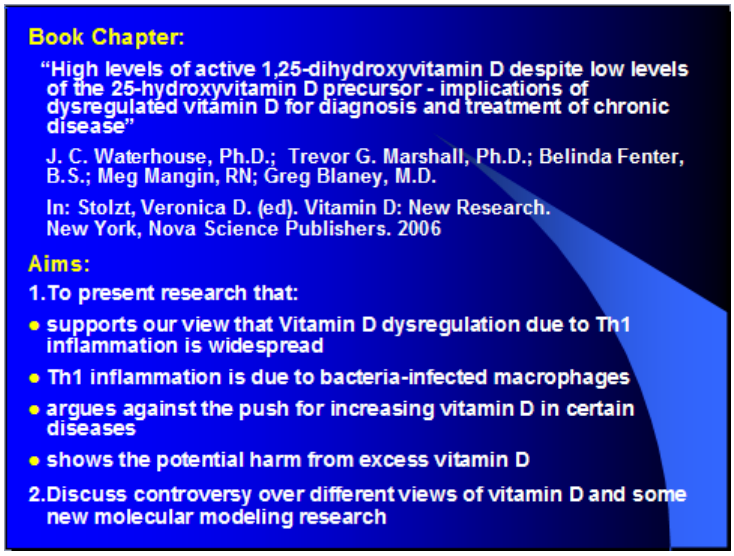
Title Slide

Hi. I hope your coffee break has you all alert enough that I won't put you to sleep. Actually, I think there is some exciting new information here, and I hope it will interest you.

The title here refers to vitamins D, no that isn't a typo, we use vitamins D since there are many forms of vitamin D. Actually, it is not really a true vitamin, since our bodies produce it, with the aid of the sun. It is actually better, in our view, to think in terms of a steroid hormone and it's precursors.

You might ask, why is vitamin D important? As you probably know, the Marshall Protocol or MP that we have been discussing at this conference includes a reduction of vitamin D to help improve immune function and bacterial killing. We need to discuss this in detail because there are widespread misunderstandings about vitamin D among people who are not aware of the true importance of some recent discoveries.

There are some researchers that seem to be saying we all need to take more vitamin D and we think this is wrong and this presentation will explain why.

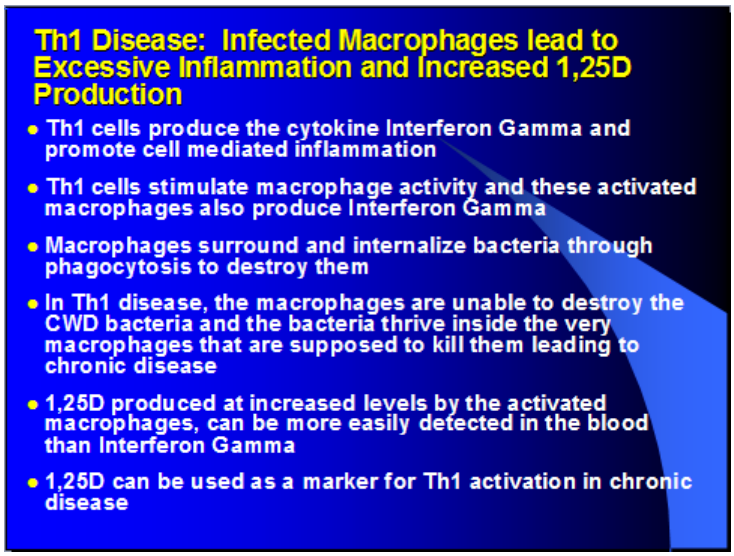


Slide 2
Book Chapter

I'm going to talk mostly today about the material covered in a book chapter, "High levels of active 1,25D despite low levels of the 25D precursor — implications of dysregulated vitamin D for diagnosis and treatment of chronic disease." It should be coming out in a month or so.

I will present research to back our view that Vitamin D dysregulation due to Th1 inflammation is widespread and is a result of macrophages becoming infected with cell wall deficient or CWD forms of bacteria. I will present evidence and arguments to counter many of the studies behind the push for increasing vitamin D in certain diseases and show the potential harm from excess vitamin D. I will also discuss the controversy over different views of Vitamin D and some very new molecular modeling results.

I won't have time for questions at the end of the talk, but you can ask me questions afterwards individually or email me at jcw@autoimmunityresearch.org. By the way, you should all have handouts of the slides to make it a little easier.



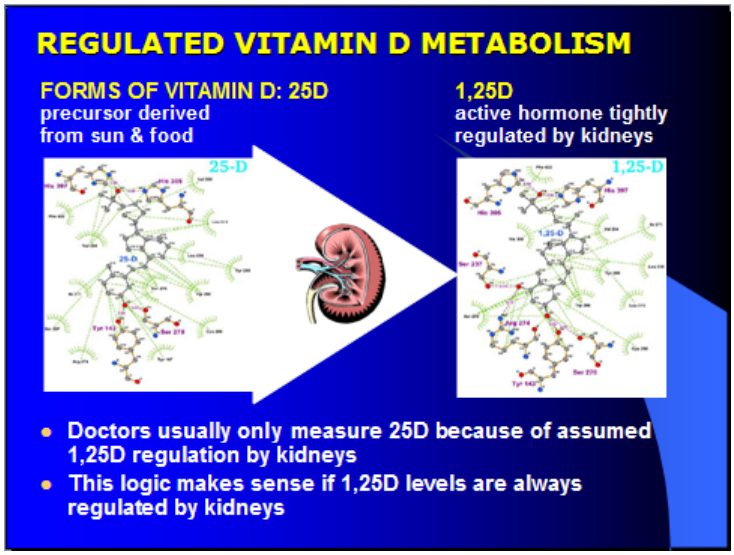
Slide 3
Th1 Disease: Infected Macrophages lead to Excessive Inflammation and Increased 1,25D Production

Now, I'll briefly go into some background information in simplified form. In our view, the key to Th1 disease is bacteria-infected macrophages leading to excessive inflammation and increased 1,25D production. Th1 cells, a type of T helper lymphocyte, or immune cell, produce the cytokine Interferon Gamma and promote cell mediated inflammation.

Th1 cells can stimulate macrophage activity and these activated macrophages also produce Interferon Gamma. The macrophages are supposed to surround and internalize the bacteria in order to destroy them, a process called phagocytosis.

Our understanding of Th1 disease is that the macrophages are unable to destroy the CWD bacteria during phagocytosis and instead the bacteria actually thrive inside the very macrophages that are supposed to kill them, leading to chronic disease.

Although elevated Interferon Gamma can indicate Th1 disease, it stays mainly in the tissue, and only circulates in the blood to a limited degree. However, the 1,25D produced by the activated macrophages, can be more easily detected in the blood than Interferon Gamma. Thus, 1,25D, can serve as a useful marker or indicator of Th1 disease and that is why we measure it, along with 25D.



Slide 4
Regulated Vitamin D Metabolism

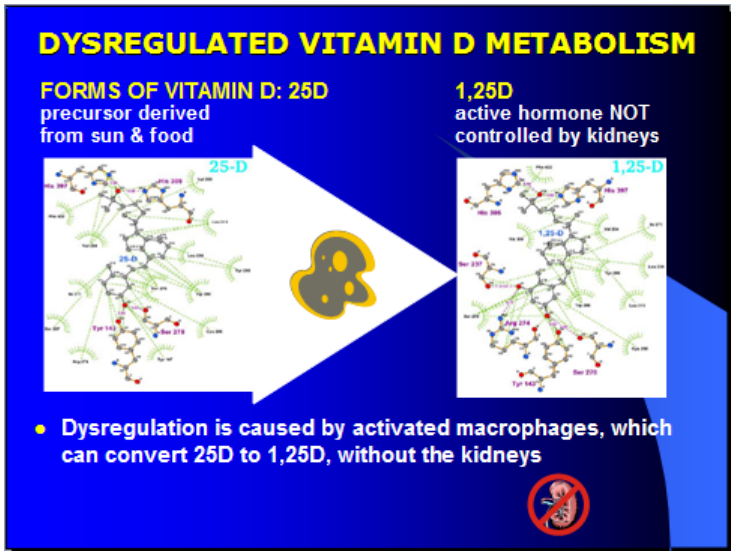
Now, on to vitamin D regulation.

This first part of the slide shows a simplified view of the vitamin D situation in a healthy person. The precursor form of vitamin D, 25D, is the form that most healthy people derive from the diet, supplements and sun exposure. By the way, this shows the situation without the inflammatory cytokines that cause the 25D from the sun to convert directly to 1,25D in the skin.

The main point to emphasize here, is that in healthy people, the kidneys tightly regulate the conversion of 25D to keep the 1,25D active steroid hormone in a fairly narrow range. There are parts of other molecules shown here — the vitamin D receptor around here, but this is the vitamin D part.

But the only difference is where you add the hydroxyl group, which is this little red oxygen. It's actually an OH and this is added and it makes all the difference. And here we have a nice picture of a kidney. O.K. So we have the molecule is transformed by adding the hydroxyl group so it can now activate the vitamin D receptor.

Most doctors rely on the 25D precursor to decide how much vitamin D is needed, without paying enough attention to the active hormonal form. This only makes sense if one assumes 1,25D levels are regulated by the kidneys with the aid of parathyroid hormone.



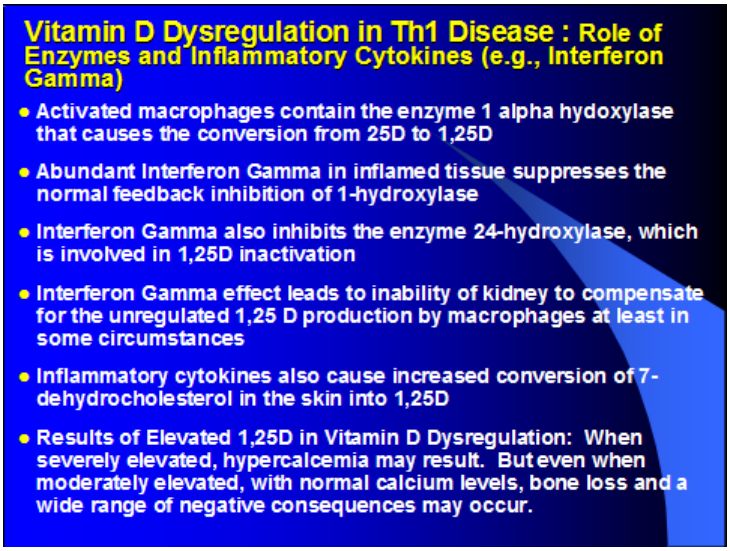
Slide 5
Dysregulated Vitamin D Metabolism

O.K., Now for the vitamin D dysregulation. Dysregulation is caused by activated macrophages, which can convert 25D to

1,25D without the kidneys, at a high rate — there you can see the macrophage.

So, the macrophages are the source of vitamin D dysregulation in Th1 diseases, aka vitamin D hypersensitivity.

This extrarenal, meaning outside of the kidneys, production is well-known in sarcoidosis and other diseases where aggregations of macrophages form granulomas. And as I said before, in Th1 disease, the 25D from the sun goes immediately to 1,25D in the skin.



Slide 6
Vitamin D Dysregulation in Th1 Disease — Role of Enzymes and Inflammatory Cytokines (e.g., Interferon Gamma)

Now, you might ask, how does Vitamin D regulation break down? Normally, there are feedback controls that would compensate for overproduction.

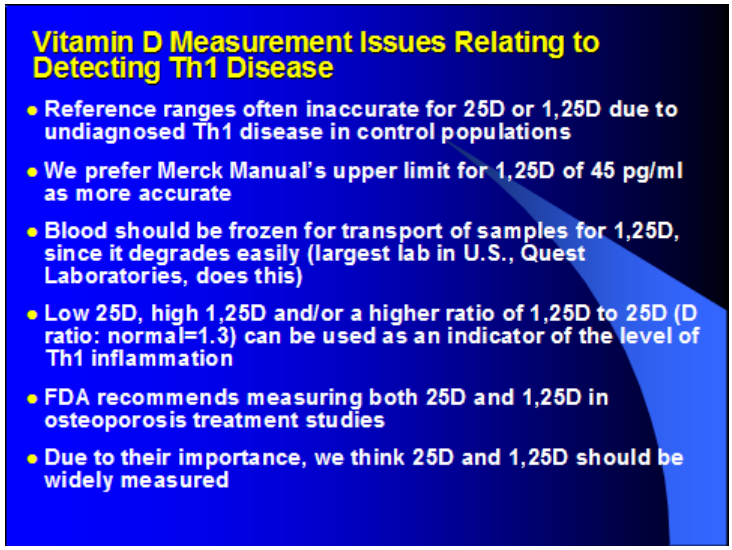
Well, it turns out we know the enzymes and cytokines involved in this failure to compensate for the macrophage's production of 1,25D.

Activated macrophages contain the enzyme 1 alpha hydroxylase that causes the conversion of 25D to 1,25D. Abundant Interferon Gamma, an inflammatory cytokine, can suppress the normal feedback inhibition of 1 alpha hydroxylase that would otherwise help regulate 1,25D production. The Interferon Gamma in the region of inflamed tissue inhibits the enzyme 24-hydroxylase, which is involved in 1,25D inactivation.

This effect of Interferon Gamma seems to extend to the kidneys, at least in many granulomatous diseases, like sarcoidosis, so that the kidney can not effectively compensate for the unregulated 1,25D production by macrophages.

Also, inflammatory cytokines cause increased conversion of 7-dehydrocholesterol into 1,25D in the skin, thus providing additional 1,25D that contributes to dysregulation.

And what is the result? Well when 1,25D is severely elevated, high blood calcium levels can occur, which may be quite dangerous. But even when 1,25D is moderately elevated, with normal serum calcium levels, bone loss and a wide range of negative consequences may occur.



Slide 7
Vitamin D Measurement Issues Relating to Detecting Th1 Disease

Now, we'll briefly cover some issues relating to measurement. We think many labs reference ranges are inaccurate because they include undiagnosed Th1 disease patients in their control populations.

For this reason, we prefer Merck Manual's upper limit of 45 pg/ml for 1,25D, to the higher upper limits some labs use.

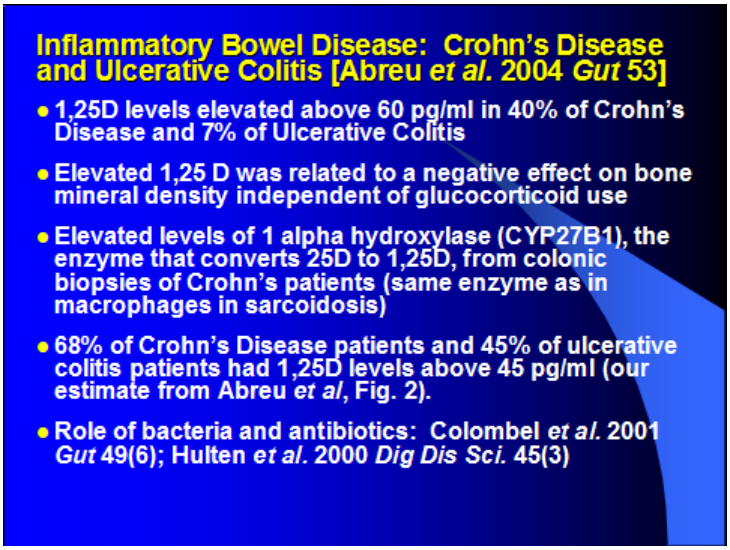
Blood serum for 1,25D tests should be frozen since 1,25D degrades easily. The largest U.S. lab does it this way.

In D dysregulation, the 25D may become depleted through conversion to the active hormone. So 25D may be low while

1,25D may be high, thus one can see the need to measure both.

Low 25D, high 1,25D and/or a higher ratio of 1,25D to 25D, known as the D ratio, can be used as an indicator of the level of Th1 inflammation. The D-ratio from a large control population that we use as "normal" is 1.3.

The FDA recommends measuring both types of vitamin D when evaluating osteoporosis treatments. We think both tests should also be much more widely done in chronic disease.



Slide 8
Inflammatory Bowel Disease: Crohn's Disease and Ulcerative Colitis...

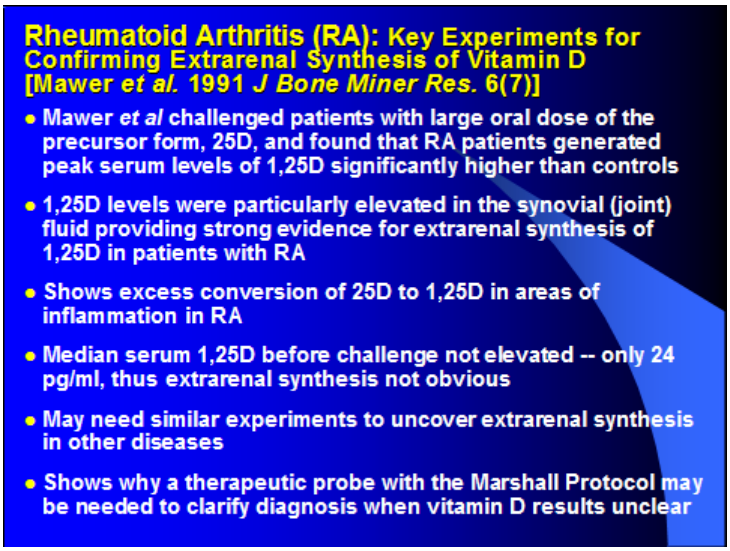
Now, I am going to review literature that supports our view that D dysregulation due to activated macrophages is actually widespread in inflammatory diseases.

In most of these diseases there is also some evidence of bacterial involvement and/or responsiveness to antibiotics. The first example is Inflammatory Bowel Diseases.

Abreu et al found 1,25D levels were elevated above 60 pg/ml in 40% of Crohn's Disease and 7% of Ulcerative Colitis patients. The elevated 1,25D was related to reduced bone mineral density that was independent of glucocorticoid use. They also found elevated levels of 1 alpha hydroxylase from colonic biopsies of Crohn's patients, indicating extrarenal synthesis, as in sarcoidosis.

The percentages are much higher if the Merck Manual cutoff for elevated 1,25D, of 45 pg/ml is used — 68% for Crohn's and 45% for Ulcerative colitis.

For the role of bacteria, you can see Colombel et al and Hulten *et al*.



Slide 9
Rheumatoid Arthritis (RA): Key Experiments Confirming Extrarenal Synthesis of Vitamin D...

Now, I will discuss a key experiment supporting extrarenal synthesis of 1,25D in rheumatoid arthritis.

Mawer et al challenged 19 RA patients with a large dose of the precursor, 25D, and found that patients generated peak serum levels of 1,25D significantly higher than controls.

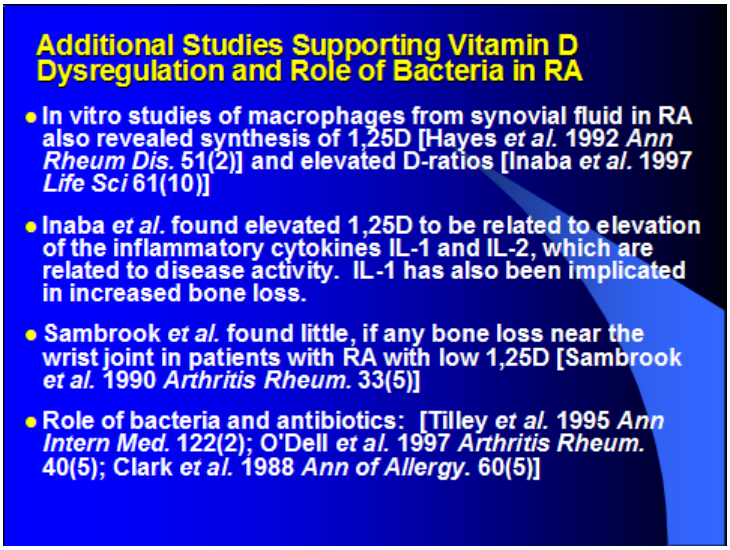
The 1,25D levels were particularly elevated in the joint fluid in patients. This provides strong evidence for extrarenal synthesis of 1,25D in patients with RA.

Another important point is that the median serum 1,25D at baseline was not elevated in the RA patients — only 24 pg/ml. Thus the extrarenal synthesis of 1,25D was not obvious from the routine blood test.

So, although we do find Vitamin D tests helpful in diagnosis, this study shows that they are not always enough. One may need to look deeper to detect extrarenal synthesis in Th1 disease.

It is also the reason why a therapeutic probe with the Marshall Protocol may be needed, when the clinical picture suggests Th1

disease, but the vitamin D test results are unclear. A therapeutic trial is when one uses the MP, and assess symptom changes — like bacterial die off reactions — to determine if the protocol is appropriate.



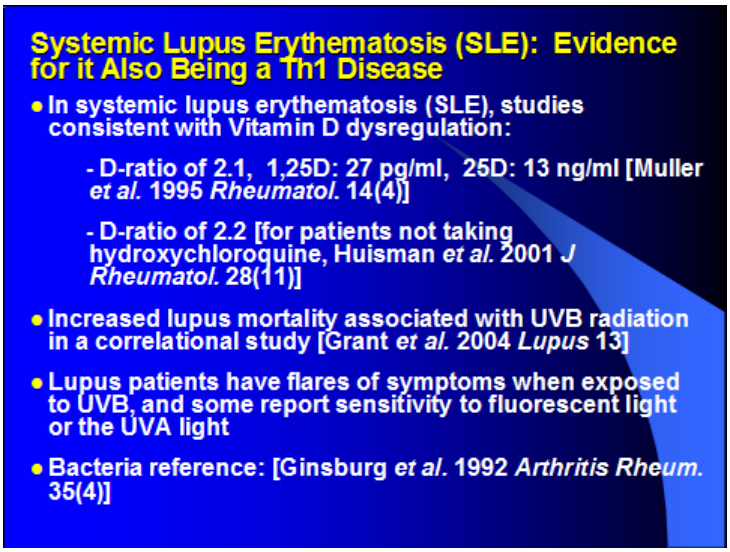
Slide 10
Additional Studies Supporting Vitamin D Dysregulation and Role of Bacteria in RA

Some additional independent studies in RA are also relevant here.

In vitro studies of macrophages from synovial fluid or joint fluid in RA also revealed synthesis of 1,25D and elevated D-ratios. Inaba found elevated 1,25D to be related to elevation of IL-1 and IL-2. These 2 inflammatory cytokines are correlated with disease activity. IL-1 has also been implicated in increased bone loss.

Sambrook et al found little, if any bone loss near the wrist joint in patients with RA with the lowest 1,25D. Those with higher 1,25D had significant bone loss near their wrist joints.

In our view, these various findings argue against vitamin D supplementation to prevent inflammatory damage or bone loss in RA. The role of bacteria and antibiotics shown in several studies further support our view that RA is similar to sarcoidosis in its underlying bacterial cause.

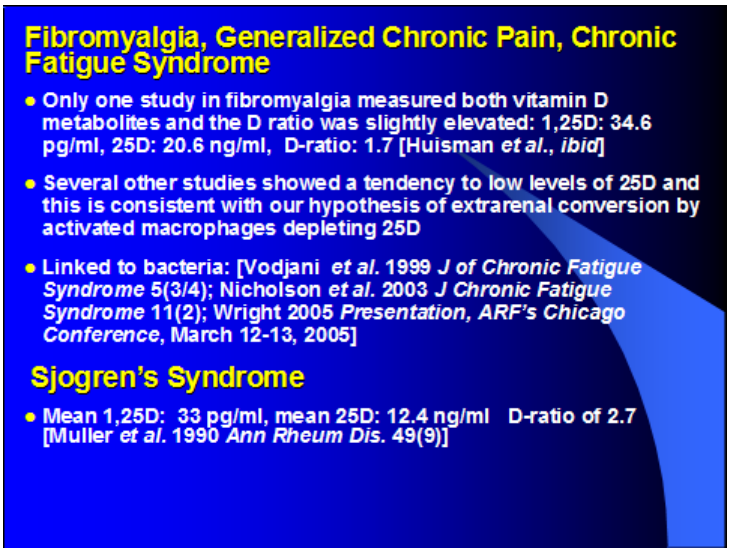


Slide 11
Systemic Lupus Erythematosis (SLE): Evidence for it Also Being a Th1 Disease

O.K., as for lupus, two studies measuring vitamin D levels are consistent with Vitamin D dysregulation, giving D-ratios of 2.1 and 2.2, well above the 1.3 average for the healthy.

Interestingly, increased lupus mortality has been found to be associated with UVB solar radiation in a correlational study and we believe this effect probably occurs through increasing 1,25D.

It is known that lupus patients have flares of symptoms in response to UVB light, and sometimes even to fluorescent or UVA light, something we observe in sarcoidosis. There was at least one study that seems to support the role of bacteria. From all of this, we conclude lupus (SLE) is a Th1 disease.

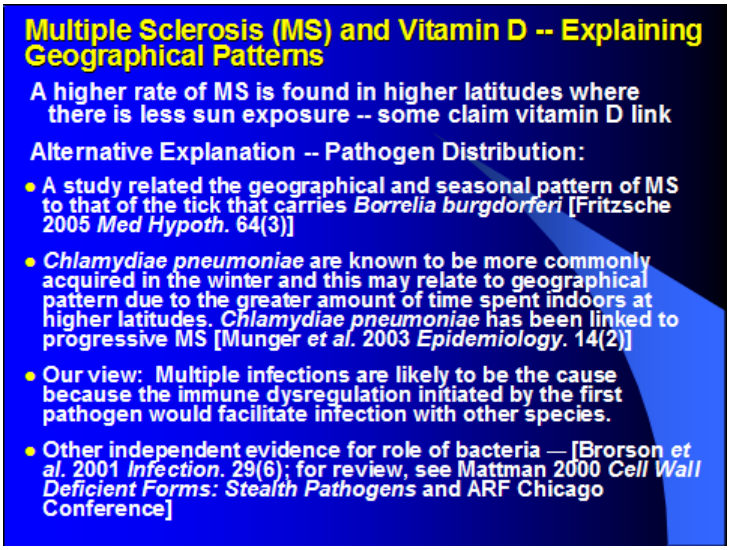


Slide 12
Fibromyalgia, Generalized Chronic Pain, Chronic Fatigue Syndrome

Only one study in fibromyalgia measured both vitamin D forms and the D ratio was elevated at 1.7.

Several other studies showed a tendency to low levels of 25D in these several chronic pain and fatigue states and this is consistent with our hypothesis of extrarenal conversion by activated macrophages depleting 25D.

Several researchers have linked chronic fatigue syndrome and fibromyalgia with bacteria, including Borrelia and Mycoplasma. Now, in Sjogren's Syndrome, the D-ratio was 2.7 and the study authors mentioned this indicated a disturbed vitamin D metabolism.



Slide 13
Multiple Sclerosis (MS) and Vitamin D: Explaining Geographical Patterns

O.K. Multiple Sclerosis. We have shown some vitamin D patterns and how they relate to our view that bacterial infection causes vitamin D dysregulation. In Multiple sclerosis or MS, vitamin D data is lacking, but there are other types of studies that have been used to try to link MS with a lack of vitamin D. And I will discuss some of the problems we see with these studies.

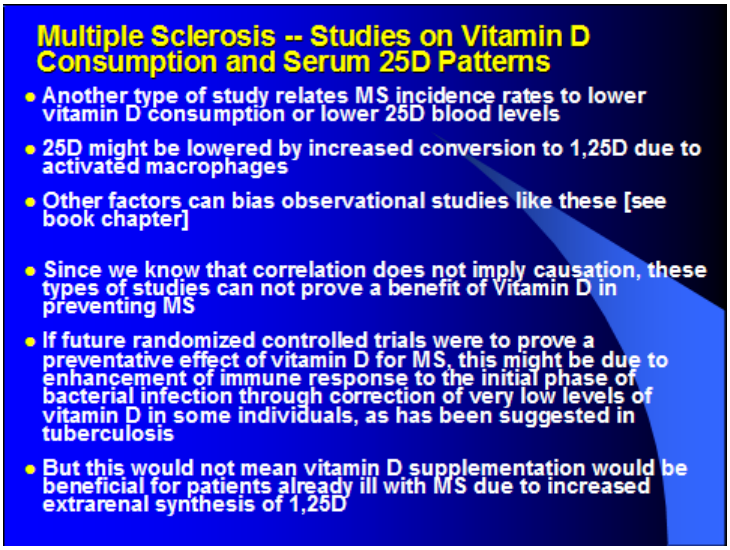
The initial reason for the interest in vitamin D in MS is that a higher rate of disease had been observed in higher latitudes — and it has been claimed that this is due to less sun exposure producing less vitamin D.

We will focus on one of the alternative explanations — that the pattern is caused by the geographic distribution of bacterial pathogens not solar radiation. An analysis by Fritzsche related the geographical and seasonal pattern of MS to that of the tick that carries the Lyme spirochete Borrelia burgdorferi.

Also, Chlamydiae pneumoniae is known to be more commonly acquired in the winter and this may relate to geographical patterns due to the greater amount of time spent indoors at higher latitudes. Chlamydiae pneumoniae has been linked to progressive MS by Munger et al.

Our view is that multiple bacterial pathogens are probably the cause of MS and other Th1 diseases. This seems likely because immune dysregulation initiated by the first pathogen would tend to promote infection with other species.

There is also abundant direct evidence for the role of bacteria in MS, for example, see Brorson et al and Mattman. Mattman has some reviews of numerous studies.

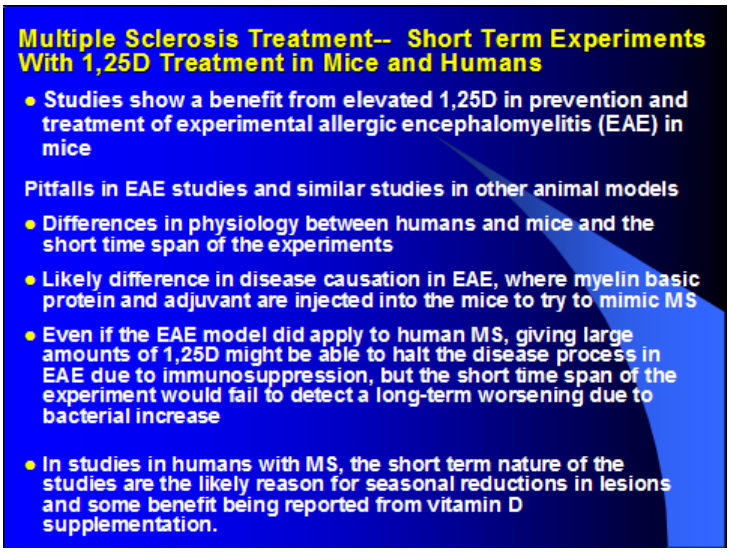


Slide 14
Multiple Sclerosis — Studies on Vitamin D Consumption and Serum 25D Patterns

Some studies have been done linking low vitamin D consumption and serum 25D patterns to a greater rate of MS. One reason we think low 25D might be observed to precede MS is increased conversion of 25D to 1,25D by macrophages thus depleting 25D in early stages of illness prior to being diagnosed — the low 25D is thus not a cause but an early effect of MS.

There are other factors that may bias results and you can see the book chapter for some examples. Since we know that correlation does not imply causation, these types of observational studies, by their very nature, can not prove a benefit of Vitamin D in preventing MS.

But, if future randomized controlled trials were to show a preventative effect of vitamin D for MS, this might be due to enhancement of immune response to the initial phase of bacterial infection through correction of very low levels of vitamin D in certain individuals. There is some limited evidence for this in Tuberculosis. But even if this preventative effect were proven, this would not mean vitamin D supplementation would be beneficial in patients already ill with MS, since, in our view, increased 1,25D synthesis would be occurring once the illness is established.



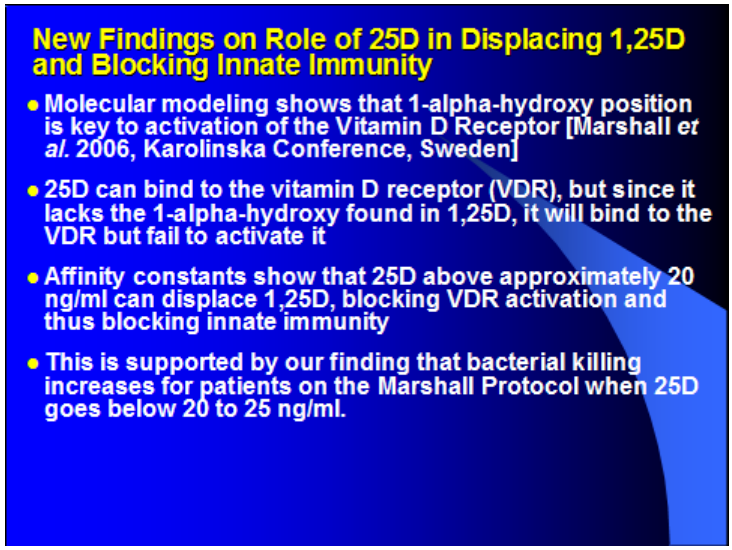
Slide 15
Multiple Sclerosis Treatment — Short Term Experiments with 1,25D Treatment in Mice and Humans

Another type of study that has been done in MS involves short term experiments in which some form of vitamin D is given.

Several studies have shown a benefit from elevated 1,25D in prevention and treatment of experimental allergic encephalomyelitis, EAE, in mice. This is an animal model used to try to approximate MS.

Some of the pitfalls of studies of this type include differences in the physiology of humans and mice and the short time span of the experiment. There is also likely to be different disease causation involved in EAE. Even if a given animal model, such as this one, did apply to human MS, giving large amounts of 1,25D might be able to halt the disease process in EAE only due to immunosuppression. But the short time span of the experiment would fail to detect a long-term worsening that might occur due to bacterial increase occurring as a result of the immunosuppression.

Likewise, in studies in humans with MS, we view the short term nature of the few studies that have been done as the likely reason that benefit has sometimes been linked to vitamin D.

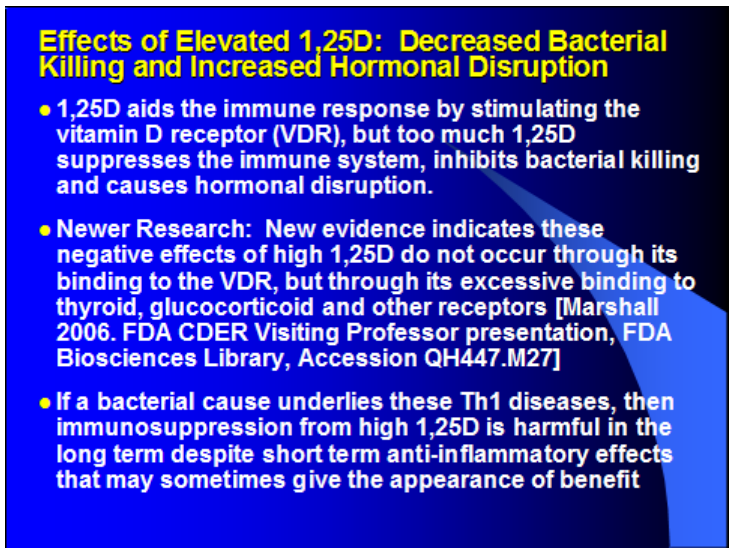


Slide 16
New Findings on Role of 25D in Displacing 1,25D and Blocking Innate Immunity

Now, I will discuss some new research on the mechanisms by which we think too much of either form of Vitamin D may suppress bacterial killing and harm long term health in Th1 disease.

Recent molecular modeling research indicates that high 25D levels block innate immunity. Sophisticated computer modeling of the molecules shows that the 1-alpha-hydroxy position is key to activation of the Vitamin D Receptor or VDR. 25D can bind to the VDR, but since it lacks the 1-alpha-hydroxy found in 1,25D, it will bind to the VDR but fail to activate it.

The affinity constants show that 25D above approximately 20 ng/ml can thus displace 1,25D, blocking VDR (Vitamin D Receptor) activation and thus blocking innate immunity. This is supported by our finding that bacterial killing increases for patients on the Marshall Protocol when 25D goes below 20 to 25 ng/ml.



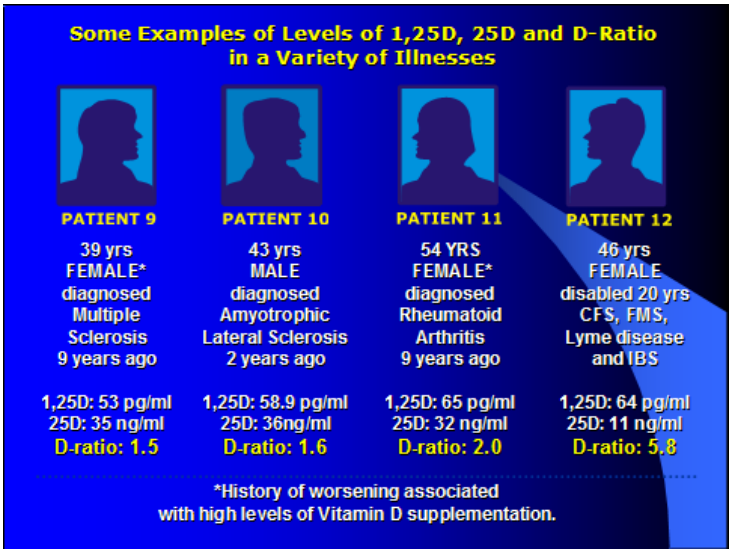
Slide 17
Effects of Elevated 1,25D: Decreased Bacterial Killing and Increased Hormonal Disruption

As for 1,25D, although it aids the immune response by stimulating the vitamin D receptor, too much 1,25D suppresses the immune system, inhibits bacterial killing and causes hormonal disruption.

New evidence indicates these negative effects of high 1,25D do not occur through its binding to the VDR, but through its excessive binding to thyroid, glucocorticoid and other receptors. Dr. Marshall has recently presented molecular modeling evidence for this at an FDA Visiting Professor presentation.

If, as we believe, a bacterial cause underlies these Th1 diseases, then immunosuppression from high 1,25D is harmful in the long

term, despite short term anti inflammatory effects that may sometimes give the appearance of benefit.



Slide 18
Some Examples of 1,25D, 25D and D-Ratio in a Variety of Illnesses

O.K. Theses are not real portraits of the people — so, you don't need to go around looking for the silhouettes to match it.

Most of the data collected on hundreds of patients — prior to starting the MP — is fitting the pattern of vitamin D dysregulation that we described above, indicating increased production of 1,25D by macrophages. Dr. Marshall presented slides of some of this data on sarcoidosis, RA, Lyme, CFS and fibromyalgia at the Chicago Conference and elsewhere.

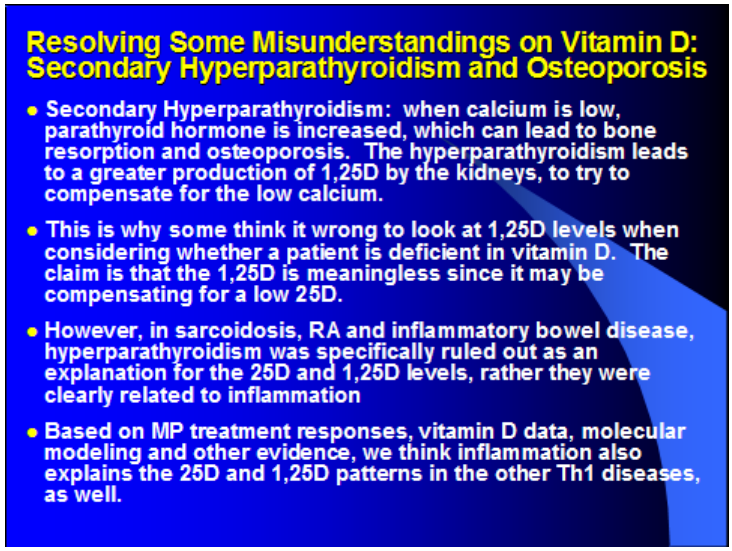
Today, I will just talk briefly about 4 of the 12 patients we discuss in the book chapter to illustrate the pattern of vitamin D values in a variety of illnesses.

In some cases, the 25D is somewhat elevated. Usually this is due to vitamin D in food or supplements, and it tends to bias the D-ratio downward. Patient 9 has MS, diagnosed 9 years ago. One can see her 1,25D of 53 is above the Merck upper limit and her 25D is rather high at 35 ng/ml and her ratio is a little elevated at 1.5. She has a history of worsening on daily doses of 2000-4000 IU vitamin D. And one symptom that had worsened while on the vitamin D improved after stopping it prior to the Marshall Protocol.

Patient 10 has amyotrophic lateral sclerosis or ALS. He has an elevated 1,25D of 58.9, a 25D of 36 ng/ml and a D ratio of 1.6. Both patients 9 & 10 have had bacterial die-off reactions, also called Jarisch Herxheimer reactions, as expected on the Marshall Protocol, but it is too soon to know if they have improved.

Patient 11 has rheumatoid arthritis and had an initial 1,25D of 65, 25D of 32, and a D ratio of 2. During 2 years on vitamin D supplementation prior to the Marshall Protocol, her condition worsened. Also, she failed to improve during several years on an antibiotic-only protocol, but improved significantly on the Marshall Protocol in less than 18 months.

Patient 12 has been disabled for 20 years by chronic fatigue syndrome, fibromyalgia and Lyme disease. With her 1,25D at 64 and her 25D at only 11, giving a ratio of 5.8, this patient is a good example of 25D being depleted by conversion to 1,25D. Sun exposure elevates her heart rate and worsens a number of other symptoms. She has improved considerably on the MP.



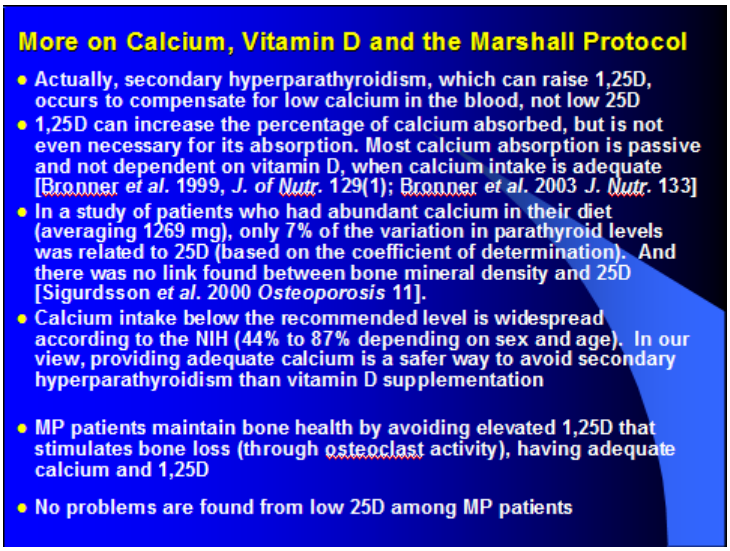
Slide 19
Resolving Some Misunderstandings on Vitamin D: Secondary Hyperparathyroidism and Osteoporosis

O.K., as to the controversy on vitamin D. Why do some advocate taking so much vitamin D and why do we think they are wrong?

To begin with, many vitamin D advocates focus on the issue of secondary hyperparathyroidism, which occurs when serum calcium is low, causing parathyroid hormone to increase, which can lead to bone resorption and osteoporosis. The hyperparathyroidism leads to a greater production of 1,25D by the kidneys, to try to compensate for the low calcium.

This is why some researchers think it wrong to look at 1,25D levels when considering whether a patient is deficient in vitamin D. Their claim is that the 1,25D is meaningless, since it may be compensating for a low 25D.

Of course, we agree that secondary hyperparathyroidism certainly can lead to bone loss. However, in several Th1 diseases we have discussed, sarcoidosis, RA and Inflammatory Bowel Disease, any hyperparathyroidism was specifically ruled out as an explanation for the patterns. Rather, the Vitamin D results were clearly related to inflammation. We think that evidence points to inflammation as the explanation of the vitamin D patterns in the other Th1 diseases, as well.

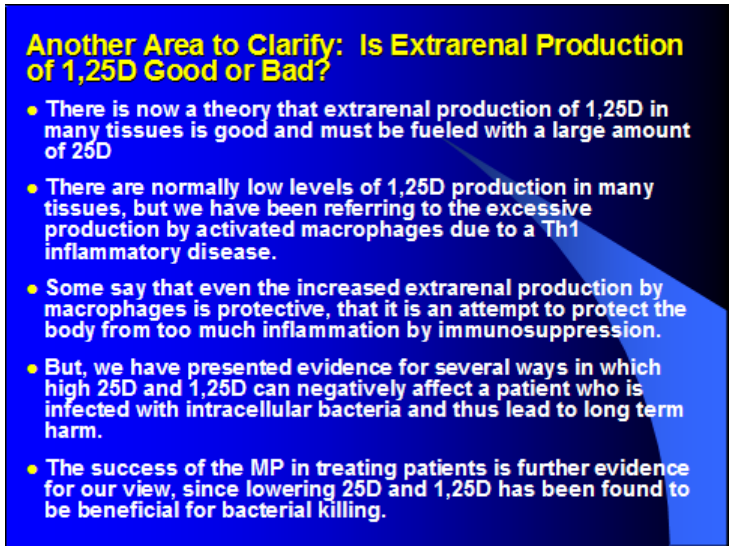


Slide 20
More on Calcium, Vitamin D and the Marshall Protocol

To clarify a little further, secondary hyperparathyroidism occurs in order to compensate for low calcium, not low 25D. The 1,25D can increase the percentage of calcium absorbed, but is not even necessary for its absorption, since when calcium is adequate, most of the absorption is passive.

The role of calcium is shown in a study of patients who had abundant calcium in their diet, and it was found that only 7% of the variation in parathyroid levels was related to 25D. And there was no link between bone mineral density and 25D. It turns out that calcium intake below the recommended level is widespread according to the NIH, varying from 44% to 87% depending on sex and age.

And in our view providing adequate calcium is a safer way to avoid secondary hyperparathyroidism than vitamin D supplementation. MP patients maintain bone health by first avoiding elevated 1,25D that stimulates bone loss through osteoclast activity and by having adequate calcium and just generally keeping 1,25D in the normal range. We have observed no problems from even quite low 25D levels among MP patients.



Slide 21
Another Area to Clarify: Is Extrarenal Production of 1,25D Good or Bad?

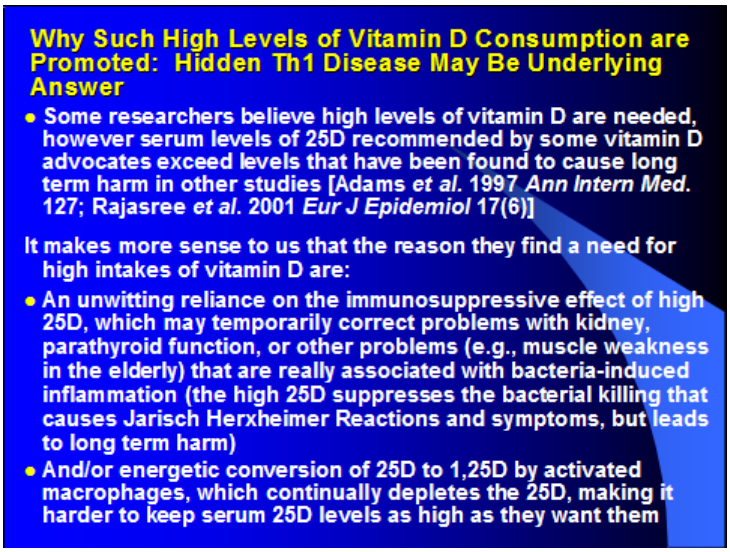
Another area that needs to be clarified is the question of whether extrarenal production of 1,25D is good or bad. The answer is it depends on how much and what is the source.

There is now a theory that a lot of extrarenal production of 1,25D in many tissues is important and must be fueled with a large level of 25D. Now there are normally low levels of 1,25D production by many types of cells and that is fine and normal. But we have been referring to something different — to the excessive production of 1,25D by macrophages in a Th1 disease.

Well, some say that even this increased 1,25D production by macrophages is good — that it is an attempt to protect the body from too much inflammation by suppressing the immune system.

But, we think this idea falls apart if we are dealing with a chronic infection. We have presented evidence for several ways in which high 25D and 1,25D can negatively affect the immune system's ability to fight CWD bacteria and thus lead to long term harm.

The success of the MP in treating patients is further evidence for our view, since lowering vitamin D has been found to be beneficial for bacterial killing.

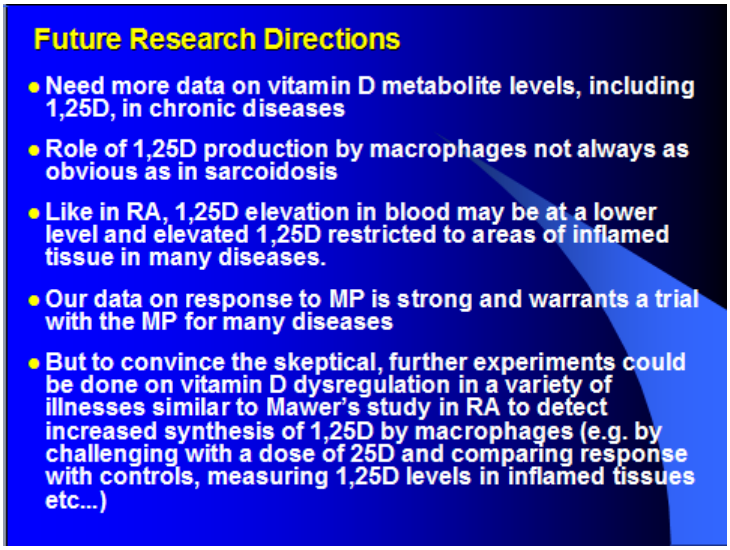


Slide 22
Why Such High Levels of Vitamin D Consumption are Promoted: Hidden Th1 Disease May be Underlying Answer

Some vitamin D proponents believe that very high levels of vitamin D are needed, levels that may exceed those found to cause harm in some studies. How could it be that some seem to find a benefit? In the light of what we know, it makes the most sense to us that the reason they find a need for high intakes of vitamin D are two fold.

They may be unwittingly be relying on the immunosuppressive or anti-inflammatory effect of high 25D, which may temporarily correct problems with kidney, parathyroid function, or other problems that are really associated with bacteria-induced inflammation. The high 25D they achieve suppresses the bacterial killing and associated die off reactions and may cause some short term benefit, but long term harm. This explanation may even apply to some elderly patients who seem to have improved muscle strength when given vitamin D.

Another reason some vitamin D advocates may find they require such high vitamin D intakes is that conversion to 1,25D by macrophages continually depletes the 25D in Th1 disease, making it harder to keep serum levels of 25D as high as they want them.

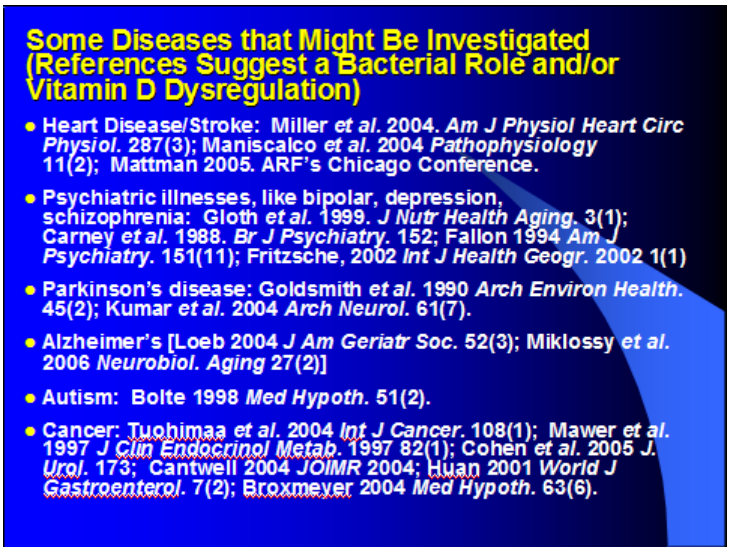


Slide 23
Future Research Directions

As for future research directions, there is a need for more data on 25D and 1,25D levels.

But, as we have shown, the role of 1,25D production by macrophages is not always obvious from simple blood tests. In the less clear cut cases, as in rheumatoid arthritis, 1,25D elevation may be at a lower level and more restricted to areas of inflamed tissue and thus not show up in the blood test.

Despite our belief that the response so far to the MP is strong enough to warrant immediate trials for many diseases, further experiments on vitamin D might be useful. Experiments could be done to detect increased synthesis of 1,25D by macrophages by challenging with a dose of 25D and comparing responses with controls — and then looking at levels of 25D and 1,25D in inflamed tissues and so on, like the experiments discussed earlier in RA.



Slide 24
Some Diseases that Might Be Investigated (References Suggest a Bacterial Role and/or Vitamin D Dysregulation)

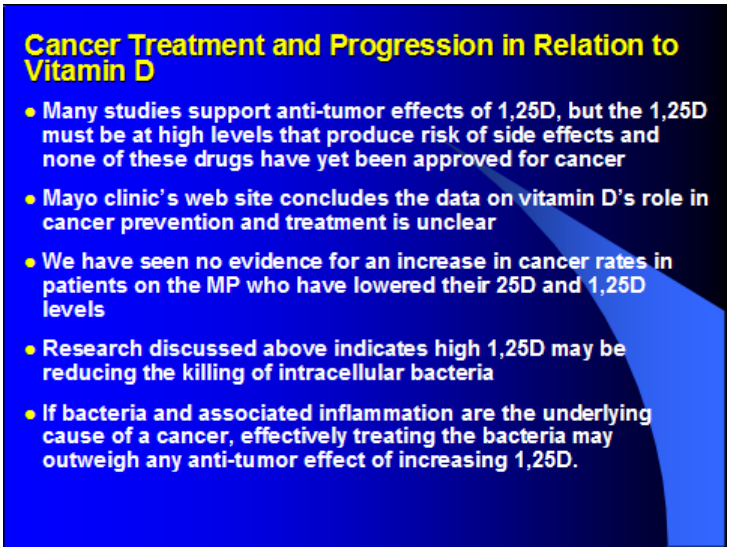
What other diseases might be good candidates for this type of investigation? The answer is, basically, any chronic disease with unknown cause.

But especially diseases where some link to vitamin D has been found — either a positive or negative effect, since this might be a sign of increased synthesis of 1,25D by macrophages.

Examples of some of the diseases that might have Vitamin D dysregulation include: heart disease and stroke; psychiatric illnesses, like bipolar, depression and schizophrenia; Parkinson's Disease; Alzheimer's; autism and cancer.

Listed on the slide are studies that find evidence suggesting a role for bacterial pathogens or a beneficial effect of antibiotics or suggestions of vitamin D having a positive or negative effect.

I should mention that there has been research, mostly observational studies, that support a positive role for Vitamin D in cancer prevention. We think many of the problems with these types of studies in cancer are similar to the problems we discussed in the section on MS. And one must also be careful to distinguish the effects of calcium from that of vitamin D and oftentimes it's not clear whether it's the calcium.

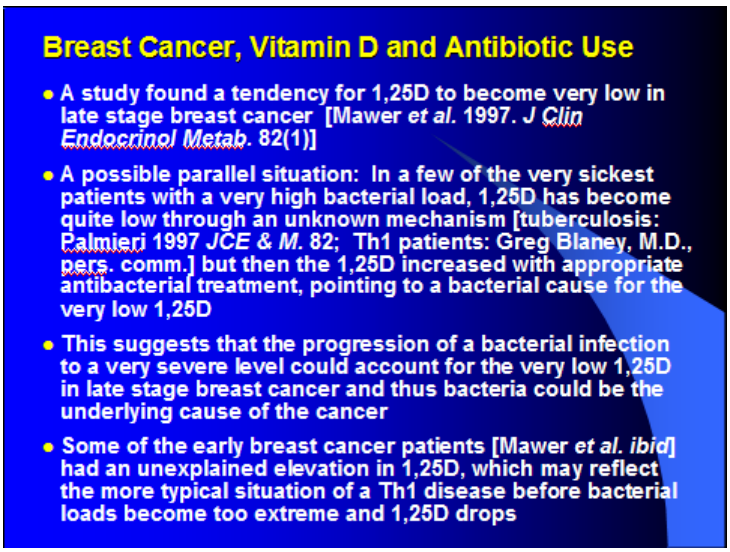


Slide 25
Cancer Treatment and Progression in Relation to Vitamin D

With regard to cancer treatment, there are many studies supporting 1,25D's anti-tumor effects. But for this effect to be useful in treatment, the 1,25D must be at high levels that produce a high risk of side effects. Neither 1,25D, nor any of the synthetic analogs created to mimic it, has yet been approved to treat cancer. The Mayo clinic, on their web site, concludes the data on vitamin D's role in cancer is still unclear.

We have seen no evidence for an increase in cancer rates in patients on the MP who have lowered their vitamin D levels. Research discussed above, shows high 1,25D may be reducing the killing of intracellular bacteria. If bacteria, and the inflammation that accompanies the bacterial infection, are the underlying cause of a cancer, then we think effectively treating the bacteria may outweigh any anti-tumor effect of increasing 1,25D.

And as was mentioned, H. pylori has been linked to ulcers, but it's also been linked to stomach cancer. So there is a clear example where the bacteria is the carcinogen.



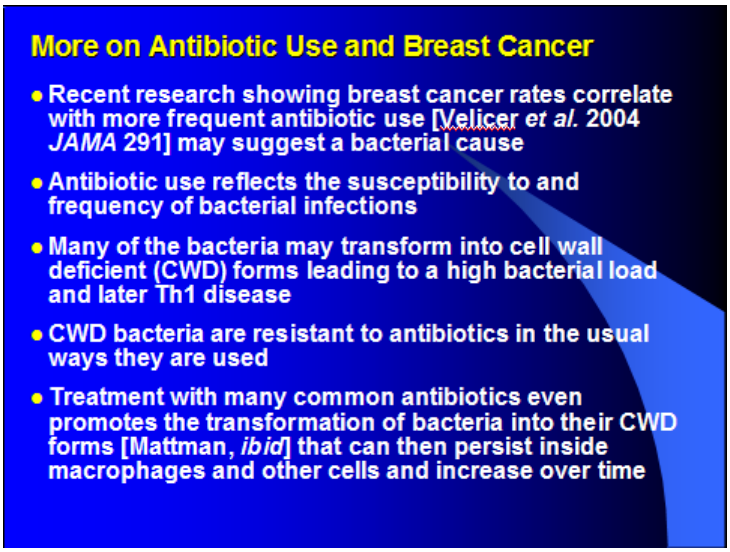
Slide 26
Breast Cancer, Vitamin D and Antibiotic Use

There is some interesting work on breast cancer and Vitamin D that may suggest bacterial involvement. There was a study that found a tendency for 1,25D to become very low in late stage breast cancer. In a possibly parallel situation, in some of the very sickest patients with a very high bacterial load, 1,25D has become quite low through an unknown mechanism.

In tuberculosis, Palmieri found this and in some Th1 patients, Dr. Blaney has found this also — this very low 1,25D also. But then, remarkably, the 1,25D increased with appropriate antibacterial treatment.

This may suggest that the progression of a bacterial infection to a very severe level could account for the very low 1,25D in late stage breast cancer and thus bacteria could be the underlying cause of the cancer. Perhaps effective antibiotic treatment for CWD bacteria could reverse the process in breast cancer and restore the 1,25D levels as it did in the tuberculosis and the very sick Th1 patients I just mentioned.

As you know from what I have said before, the 1,25D is usually elevated in Th1 disease. So it is interesting that some of the early breast cancer patients had an unexplained elevation in 1,25D, which may reflect the more typical situation of a Th1 disease before bacterial loads become too extreme and 1,25D drops.



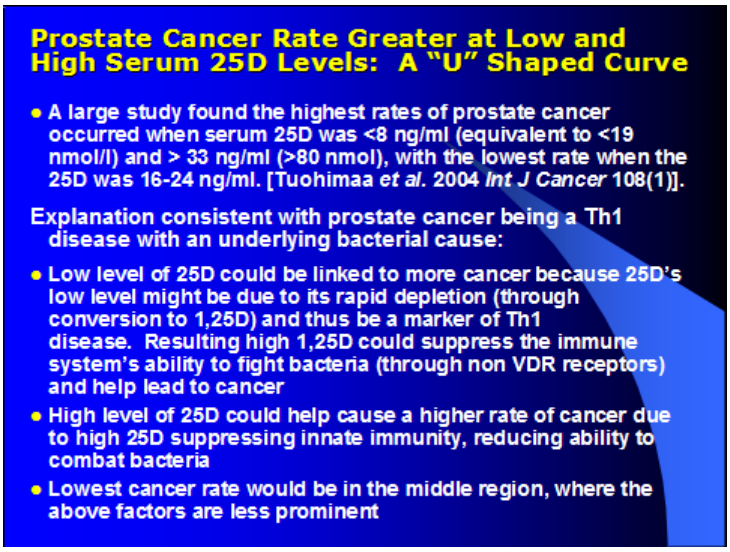
Slide 27
More on Antibiotic Use and Breast Cancer

A recent article showed breast cancer rates correlate with more frequent antibiotic use. We think this may suggest a bacterial cause for breast cancer.

In our view, antibiotic use can be thought of as reflecting the susceptibility to and frequency of bacterial infections. Many species of bacteria have been shown to be able to transform into cell wall deficient forms when under attack in order to escape destruction.

CWD bacteria are resistant to antibiotics in the usual ways they are used, so taking antibiotics will not generally eliminate them. And treatment with the most commonly used antibiotics even promotes the transformation of bacteria into their CWD forms, which can then persist inside the body inside macrophages and other cells and increase over time.

Thus, in our interpretation, the more exposure to bacteria indicated by the greater antibiotic use in the study, the more opportunities for the creation of CWD bacterial forms, which may then lead to Th1 disease and possibly to cancer.



Slide 28
Prostate Cancer Rate Greater at Low and High Serum 25D Levels: A "U" Shaped Curve

A particularly interesting, large new study on vitamin D and prostate cancer went beyond the geographical correlational studies and actually measured the 25D levels. They found that the highest rates of cancer occurred when serum 25D was low (<8 ng/ml) and when it was high (>33 ng/ml), giving a U shaped curve.

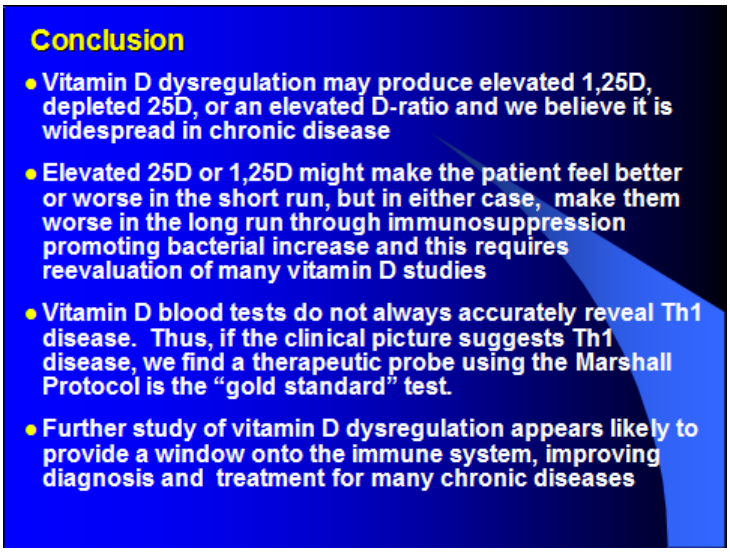
We think these patterns may indicate Th1 disease due to bacteria. Here is our hypothesis to explain this pattern. The low 25D link to cancer, rather than indicating a deficiency, could be a sign of depletion of 25D through conversion to 1,25D. Thus, it may be simply a marker for a Th1 process. As we have discussed, the resulting high 1,25D in Th1 disease suppresses the immune system's ability to fight bacteria and thus may help lead to cancer.

On the other hand, a very high level of 25D could help cause a higher rate of cancer due to the high 25D suppressing the immune system, as previously discussed. The result would then be that innate immunity is less functional and less able to combat bacteria, which may then lead to cancer.

The lowest cancer rate was in the middle region, 16-24 ng/ml, where the above two factors are least prominent. But it should be emphasized, that we do not think this data shows that the optimal level of 25D is in the middle region. In our view, the low 25D is linked to cancer merely because it is a marker of Th1 disease, not a causal factor.

The authors of the prostate cancer study concluded that too high a level of 25D might increase the risk of prostate cancer. As you saw

from our patients slide, it isn't that hard to exceed 30 ng/ml of 25D, especially with vitamin D supplements — 3 of the 4 patients had levels above 30.



Slide 29
Conclusions

In conclusion, we have shown that Vitamin D dysregulation may produce patterns of elevated 1,25D, depleted 25D or an elevated D-ratio, as we show for a variety of chronic Th1 diseases.

Elevated 25D or 1,25D might make the patient feel better or worse in the short run, but in either case, make them worse in the long run. This worsening occurs through immunosuppression promoting bacterial increase.

We think the evidence for this new view of vitamin D requires re-evaluation of many previous studies and calls for new types of studies in many chronic diseases.

Although usually quite helpful, Vitamin D blood tests do not always accurately reveal Th1 disease. Thus, if the clinical picture suggests Th1 disease, we find a therapeutic probe using the Marshall Protocol as the "gold standard" test for Th1 disease and bacterial involvement.

If you think about it, it seems little wonder that vitamin D has become so popular. It's basically an over-the-counter steroid — but its effects are more subtle and insidious than something like prednisone since it blocks only innate immunity, leaving adaptive immunity intact.

We think that further study of vitamin D dysregulation appears likely to provide a window onto the immune system, improving diagnosis and treatment for many chronic diseases.

Thank you for your attention.